

METHOD AND APPARATUS FOR THE DIAGNOSIS OF GLAUCOMA AND OTHER VISUAL DISORDERS

1 Method and Apparatus for the Early and Rapid
2 Diagnosis of Glaucoma and Other Human and Higher
3 Primate Visual Disorders

4
5 This invention relates to methods and apparatus for
6 assessing eye function. The invention is useful
7 *inter alia* in the diagnosis of glaucoma and other
8 visual disorders, and in the assessment of dyslexia
9 and neurological conditions which affect eye
10 function.

11
12 The common form of glaucoma, as is typical of
13 several other visual disorders, is a progressive
14 disease. Currently the disease can be arrested but
15 not cured. Symptoms include the gradual reduction in
16 the field of view of the affected eye progressing in
17 a characteristic pattern. Due to the nature of the
18 human visual system, victims of the disease do not
19 typically notice this reduction in field of view
20 until the disease has already progressed for several
21 years. Instruments exist which can measure the
22 field of view of a patient but all available
23 instruments suffer from three major problems that
24 limit their utility in making an early diagnosis.

1 First they are both low in resolution and
2 inaccurate. This low resolution means that the slow
3 progression of the disease at typically 1.8% of the
4 field of view per annum can take several years to be
5 detectable. (See for example "Relative rates of disc
6 and field change examined in eyes at high risk"
7 C Scerra, Ophthalmology Times 15/10/2001)

8
9 Secondly the existing devices and methods are slow
10 and complex in clinical use and hence expensive in
11 practitioner time. This means that even those
12 practitioners who possess a field of view analysis
13 device cannot economically use it as a routine
14 screening device.

15
16 Thirdly the existing instruments are inherently
17 expensive and so are not as widely available as is
18 required for the widespread screening necessary for
19 early diagnosis.

20
21 At one time it was thought that measurement of
22 eyeball pressure would provide a method for early
23 diagnosis of glaucoma but this has proved unreliable
24 as the correlation between pressure and glaucoma has
25 proved not to be as high as was originally thought.
26 Instruments for the measurement and mapping of the
27 sensitivity of the human retina known as "visual
28 field analysers" or "Static Auto-perimeters" have
29 hitherto required that the subject perform very
30 unnatural and often uncomfortable eye behaviours
31 such as long periods of attempted fixation on a
32 point. Additionally, hitherto such instruments

1 depended on tests requiring a voluntary response
2 from the subject. The subject is asked to
3 concentrate on a fixation point and report on the
4 presence and position of stimuli presented to their
5 peripheral vision. This process is both slow and
6 prone to inaccuracy. The ability of the subject to
7 accurately fixate is also known to be poor
8 especially over an extended period and so the
9 accuracy of a purely fixation point to stimulus
10 measurement is further compromised.

11
12 This invention substantially reduces or eliminates
13 these problems and introduces an entirely novel
14 method and apparatus that allows the subject under
15 test to behave completely naturally (in the sense
16 that they are not required to suppress natural
17 visual reflexes) which both improves accuracy and
18 lowers the stress on the subject. Furthermore the
19 disclosed method and apparatus greatly reduces the
20 time required to map the visual field, which makes
21 the test far more economic and practical for routine
22 screening than the existing equipment that requires
23 lengthy tests under expensive expert supervision.

24

25

BACKGROUND TO THE METHOD

26 While eye to hand co-ordination and reaction is
27 relatively slow and subject to variability and
28 improvement from practice, and eye to voice reaction
29 time is even slower, the reaction time of the eye
30 itself to stimulus is extremely fast in humans and
31 primates. The eye muscles reflexively react to
32 stimuli without the need for conscious action by the

1 subject. Although this reflex can be consciously
2 overridden, the nature of the stimulus and prior
3 fixation can be engineered by methods disclosed in
4 this invention to ensure that the reliability
5 exceeds 97 percent. Furthermore, because the eye
6 reflex is inherently faster than eye-hand or eye-
7 voice reaction times, any variability in the
8 response has a far lower impact on the accuracy of a
9 reaction dependent measurement. This allows the
10 apparatus to exploit the time information in a
11 variety of ways to increase the data obtainable from
12 each individual test point.

13

14 The invention, which is defined in the appended
15 claims, is based on the use of an eye position-
16 measuring device capable of measurement of eye
17 position at intervals of less than 45 ms, of which
18 several types are commercially available, in
19 conjunction with a display unit capable of
20 displaying a multiplicity of visual stimuli and
21 capable of accurate calibration of luminance
22 sufficient to exceed the desired accuracy of the
23 desired test. The device is configured to detect the
24 rapid motion of the eye (known as a saccade) towards
25 a new stimulus and to use this saccade to determine
26 the moment the subject's visual reflex responds to
27 the stimulus. Since the subject need not consciously
28 respond to the stimuli the entire field of view
29 measurement process can be automated. By way of
30 example, a set of stimuli can be presented, each
31 stimulus initially below expected threshold
32 increasing in brightness until the stimulus triggers

1 the reflex saccade of the eye from a fixation
2 stimulus. The time the reflex saccade is detected is
3 used to determine the threshold of the retina for
4 that point. The eye position-measuring device can in
5 a preferred embodiment be used to check that the
6 eye's saccade did in fact occur in the correct
7 direction confirming that the test stimulus and not
8 another distraction caused the saccade. At the
9 moment of the said saccade the stimulus that was the
10 saccade target transforms into the fixation point
11 for the next stimulus. This is an important feature
12 for two reasons.

13

14 First, the accuracy of immediate post saccade
15 fixation has been shown to be consistently many
16 times better than long term fixation on a single
17 point, and secondly the visual process of saccading
18 from one stimulus to another in sequence is the
19 normal visual scanning mode of the human and higher
20 primate eye, hence the experience for the patient
21 feels natural and unforced, especially if the
22 frequency of the induced saccade is designed to be
23 equivalent to the normal scanning saccade frequency
24 of the eye. This normal scanning frequency varies
25 from time to time in a given individual and from
26 individual to individual but the invention also
27 discloses a method that allows the practitioner to
28 quickly determine this value accurately. Setting the
29 saccade frequency perfectly is not generally
30 necessary but will help to make the test more
31 accurate particularly with anxious patients.

32

1 A major advantage of this method of field of view
2 measurement over the prior art is that it eliminates
3 the need for very large samples to be gathered for
4 each stimulus position and repetitive confirmation
5 of the subject's observation of the stimulus and the
6 reliability of their visual fixation. This vastly
7 reduces the time needed for a diagnostician to
8 establish a subject's field of view.

9
10 In preferred forms, the invention exploits a
11 detailed computer model of the human visual system's
12 autonomic reflex timings and uses a response
13 interpolator based on this model to allow more
14 accurate interpretation and extrapolation from data
15 while ensuring that the conditions of the test more
16 closely approximate normal visual tasks. This
17 improves both the comfort of the subject and
18 accuracy of the test results. The invention allows
19 sufficient accuracy to determine progression from
20 one test to another of a fraction of a percent,
21 takes little clinical time to administer and the
22 apparatus itself is economic and easily affordable.

23
24 In addition to the above benefits the nature of the
25 disclosed method and apparatus also has utility in
26 diagnosis of other visual disorders not directly
27 related to visual field but still dependent on the
28 exploitation of the computer reflex model. This
29 allows the invention to be applied to the diagnosis
30 of high function visual disorders such as dyslexia
31 and visual "neglect". Dyslexia is a higher brain
32 function disorder, which can be improved by

1 appropriate training, and "neglect" is a symptom of
2 a particular form of brain damage.

3

4 SUMMARY OF THE INVENTION

5

6 The invention provides a method as defined in claim
7 1, apparatus as defined in claim 24, and also a
8 software package as defined in claim 42.

9

10 Preferred features of the invention and benefits
11 thereof will be apparent from the subordinate claims
12 and from the description.

13 DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE
14 INVENTION

15

16

17 Embodiments of the invention will be described, by
18 way of example only, with reference to the
19 accompanying drawings, in which:

20

21 Fig. 1 is a schematic illustration of one
22 apparatus embodying the invention; and

23 Figs. 2 and 3 represent images used in one
24 method according to the invention.

25

26 Prior to this invention visual field analysis
27 methods and apparatus have been extremely crude, in
28 general consisting of an array of lights or other
29 display illuminated under a pseudo-random protocol
30 and at varying brightness straddling the expected
31 threshold of the retina and a fixation point to
32 attempt to maintain some minimal knowledge of the

1 eyes position prior to stimulus. Unfortunately the
2 human vision system is particularly poor at
3 maintaining a constant fixation and furthermore even
4 if this is achieved with practice there are side
5 effects to concentration on a fixation point that
6 significantly reduce the accuracy of the
7 measurement. As a consequence most of these machines
8 are, in practice, little better than the intelligent
9 use of a pen waved at the subject by the
10 practitioner. They provide a rough map of defective
11 areas but the positional accuracy of the defect
12 perimeter is grossly compromised by the
13 impossibility of accurate fixation maintenance by
14 the subject and furthermore the nature of a pursuit
15 or fixed fixation task in itself causes large
16 variations in the subjects' apparent peripheral
17 retinal sensitivity. In research applications with
18 volunteer subjects who are practiced in the use of
19 the instrument these instruments do provide useful
20 data but as a routine diagnostic tool they are
21 simply too complex, time consuming and difficult to
22 use for both the practitioner and the patient.

23

24 The following references confirm this assertion:

25

26 "Selective Peripheral Fading:

27 Evidence for Inhibitory Effect of Attention on
28 Visual Sensation"

29 Lianggang Lou

30 Department of Psychology

31 The University of Hong Kong

32

1 Barbington-Smith B, 1961 "An unexpected effect of
2 attention in peripheral vision" *Nature (London)* 189
3 776

4
5 Duncan J, 1980 "The locus of interference in the
6 perception of simultaneous stimuli" *Psychological*
7 *Review* 87 272-300

8
9 The prior art of which the following small sample is
10 typical, ignores the nature of the human visual
11 system as a whole. In the absence of such a model
12 the measured values for a given point in the field
13 of view will be tend to be grossly inaccurate both
14 spatially (topologically) and in amplitude terms.
15 The results are akin to plotting the chart of a
16 shoreline with an elastic plumb line and a faulty
17 sextant.

18
19 As stated above the prior art consists primarily of
20 various methods of presenting varying brightness
21 stimuli to the eye from various angles depending on
22 some form of fixed or moving reference fixation
23 point to deliver geometric accuracy or they include
24 some form of eye tracking system which requires a
25 calibration that is itself subject to the same error
26 of fixation as the untracked test. All of the prior
27 art requires significantly abnormal eye behavior
28 from the subject under test over typically tediously
29 long periods. As the above references show such
30 abnormal fixation behavior inherently destroys both
31 the topological and amplitude accuracy of the data
32 being collected to the point where it is accepted in

1 ophthalmic diagnosis that the repeatability of the
2 measurements can not be better than plus minus 5
3 degrees and plus minus 2.5dB. Given the progress of
4 common glaucoma at 1.8 percent per annum this means
5 in practice that a confirmed diagnosis of glaucoma
6 can take the several years required to establish the
7 nature of progression with such low repeatability
8 instruments.

9

10 EXAMPLES OF THE MOST COMMONLY USED PRIOR ART

11 US4561738: Field tester
12 Humphrey; William E., San Leandro, CA
13 Campbell; Charles, Berkeley, CA
14 US5050983: Visual testing method and apparatus
15 Johnson; Chris A., Davis, CA
16 Shapiro; Lionel R., Davis, CA
17 US5024519: Apparatus and method for visual-field
18 testing
19 Howard; Dwight L., Winters, CA
20 Johnson; Chris A., Davis, CA

21

22 The present inventors theorised that if a test
23 method could be devised that allowed the patient to
24 behave as naturally as possible it would
25 consequently be true that the patient's autonomic
26 responses would more reliably follow normal
27 repeatable curves. The inventors also researched
28 both fixation and stimulus methods that promote
29 relaxed natural reflex saccades. By carefully
30 researching the limit and variability of these
31 normal responses it would be practical to gather

1 information about the eye's sensitivity and visual
2 field from careful timing of the natural saccade
3 responses to stimuli. This could be applied to
4 several visual stimuli ranging from a carefully
5 sequenced repetitive single point stimulus similar
6 to a conventional visual field analysis method to
7 the presentation of specially formatted images or
8 video sequences where the saccade timing variation
9 between a normal and a visually impaired individual
10 could be made readily apparent.

11
12 This theory was subsequently proved to both the
13 inventors' satisfaction and led to the present
14 invention.

15
16 Referring to Fig. 1, one embodiment of apparatus for
17 use in the invention comprises a display screen 10
18 viewed by a subject 12. Any suitable display may be
19 used which is capable of presenting images where the
20 luminance of any point in the image over the desired
21 field of view can be defined at least as accurately
22 as the desired amplitude accuracy of the desired
23 retinal map. Preferably, the display is capable of
24 presenting an animated fixation image consisting of
25 a substantially stationary central region comprising
26 at least 20 percent of the diameter of the fixation
27 image, and a mobile perimeter defined such that the
28 perimeter is less than 3 degrees of the arc of
29 vision of the subject in diameter. By way of
30 example, such a fixation image might consist of an
31 insect such as a ladybird with wiggling legs acting
32 as the mobile perimeter, or in a more abstract form

1 a central disc with an eccentric ring with the
2 perigee rotating about the central disc.

3
4 An eye position sensor 14 detects movement of the
5 subject's eye. The sensor should be capable of
6 measuring eye position at intervals of less than
7 45ms. Several types of sensors meeting these
8 requirements are available commercially.

9
10 The eye motion sensor typically comprises a video
11 camera connected to a computer, in combination with
12 software executed by the computer. The software
13 compares each new frame of the video output from the
14 camera to an average of a previous plurality of
15 frames, typically two to five video frames depending
16 on required sensitivity and speed of response. The
17 frames are compared in terms of each RGB value for
18 each pixel and a threshold difference is set
19 determining the change in RGB value that constitutes
20 a motion fast enough to be a saccade of the pupil.
21 The averaging of the previous group of frames
22 eliminates noise differences and the threshold
23 determines both the magnitude and speed of a motion
24 in the frame. The video cameras are mounted on a
25 headset and may be wirelessly connected to the
26 computer, suitably via a 1.2 or 2.4 GHz wireless
27 video link. Suitable cameras are available from
28 Ajoka, Swan and Sony. Sony cameras can also be run
29 at very high frame rates and so can improve
30 accuracy. The eyes are preferably illuminated with
31 infra red light so that the image is monochrome
32 whether the camera is colour or not.

1
2 A distance sensor 16 monitors the distance between
3 the subject and the display in at least the z-
4 direction (i.e., the direction orthogonal to the
5 left/right and up/down movements of the subject's
6 eye). The distance sensor is preferably one which
7 is non-contact and thus does not restrain head
8 movement, for example ultrasonic ranging, laser
9 ranging, stereo or mono video perspective analysis,
10 suitable forms of which are available commercially.
11 Contact means which do not unduly constrain head
12 movement may also be used but are not preferred.
13
14 Typically, the z-measurement is made by an
15 ultrasonic ranging system coupled to the computer
16 (e.g. via RS232), available from Miford Instruments
17 as one example. However, alternative ranging systems
18 could be used. One option is a second video camera
19 mounted on the test screen top centre and connected
20 to the computer (e.g. via USB), which detects the
21 pupils of the eyes using an infra red source co-
22 axially mounted with the camera lens via a beam
23 splitter, or simply placed as close to the lens as
24 possible. This produces bright spots at the pupils
25 as seen by the camera (the same effect that causes
26 "red eye" in a flash photograph). The camera image
27 can be adjusted via brightness and contrast and
28 suitable infra red pass filters so that only the
29 pupils are seen in the image as two bright dots.
30 Software determines the distance between the two
31 dots. Suitable software is commercially available
32 but is also easy to write from scratch. One supplier

1 of suitable software, called Common Vision Blox, is
2 Image Labs International, Montana USA, who also
3 produce software components suitable for use in the
4 motion detection previously described. In use, the
5 optician enters the Inter-Pupil Distance to the
6 system and the z-distance can then be calculated
7 from knowledge of the apparent separation of the
8 pupils, the focal length of the lens and the size of
9 the image sensor.

10

11 A control means 18 controls the display on the
12 screen 10 and receives and processes data from the
13 sensors 14 and 16, in particular data relating to
14 the timing and direction of saccades following the
15 presentation of stimuli. Comparison means 20
16 compares this data with a library of information
17 held in a database 22, and results are output to a
18 recording or display means 24. The various elements
19 18, 20, 22, 24 may suitably be incorporated within a
20 general purpose computer.

21

22 Unlike the prior art, the present invention uniquely
23 exploits an accurate model of the autonomic visual
24 reflexes and interrelated aspects of visual
25 perception in humans and higher primates to vastly
26 improve the accuracy and repeatability of the
27 measurement. This model is incorporated in the
28 timing versus illumination increments described in
29 the method. Additionally, the natural interaction of
30 the device with the subject eliminates stress and
31 fatigue in the test that further enhances the
32 repeatability. Uniquely, after rapid basic mapping

1 of the visual field the device allows the detailed
2 plotting of any portion of the retina such as the
3 perimeter of a defect to a repeatable accuracy of a
4 fraction of a degree, allowing defect progression
5 rates of 1 degree per annum or less to be detected
6 and characterised by tests separated by weeks rather
7 than years.

8
9 The models of the autonomic visual reflexes and
10 interrelated aspects of visual perception
11 incorporated in the method and apparatus include the
12 property of the human optical system that perceives
13 stimuli of higher intensity earlier than stimuli of
14 lower intensity. This effect is primarily the
15 consequence of the integrating nature of the retina.
16 The longer a given brightness shines on a given area
17 of the retina the more photons are delivered to the
18 integration until eventually the threshold is
19 crossed, the speed of transit of visual stimuli
20 through the nerve and visual cortex to the brain is
21 also varied by the relative intensity. This gives
22 rise to the phenomenon known as the "Pullfrich
23 effect" after the discoverer who described several
24 optical illusions for which the said intensity
25 dependent delay is responsible. It has been used as
26 a method for pseudo stereo image presentation. In
27 the prior art stimuli for visual field analysis have
28 been generally presented for a given fixed time as
29 well as a given brightness so that the threshold of
30 the retina could be determined. This required the
31 sequential and separate presentation of stimuli of
32 different brightness for any given point to

1 establish the threshold of the retina as in
2 US5024519 and others. Such a method is extremely
3 time consuming but hitherto the integration effect
4 precluded the possibility of simply delivering a
5 stimulus of increasing brightness at a given point
6 as there was no way to determine the precise moment
7 that the stimulus was perceived.

8
9 Conversely, in the present invention the eye's
10 saccade reflex is modeled in the computer timing so
11 that the moment of perception can be derived from
12 the time interval between the induced saccades. The
13 integration time is exploited to refine the accuracy
14 of the sensitivity measurement of the retina and
15 simultaneously minimize the duration of the test.
16 The equations below demonstrate how this is achieved
17 despite the fact that while the retinal integration
18 is exponential up to the retinal threshold the
19 Pullfrich delay continues to reduce linearly as the
20 stimulus becomes brighter. Hence the time from
21 presentation to the triggering of a saccade will be
22 tens of milliseconds longer for a dimmer stimulus
23 even if both stimuli integrate above the retinal
24 threshold in less than a millisecond. Conversely if
25 the stimuli took 200 ms or more to integrate above
26 threshold the latency delay before the saccade after
27 the retinal threshold is crossed would be much
28 longer than for the previous example so the
29 resulting total delay would be much longer
30 effectively amplifying the time difference between
31 saccades stimulated by different threshold levels of
32 different points on the retina.

1
2 In conventional static auto perimetry, stimuli are
3 presented for a fixed time and so deliver a fixed
4 energy to the retina. The patient is asked to press
5 a button or vocalise if they see a given stimulus at
6 a given point while fixating on a central fixation
7 point. Crucially they must suppress any reflex
8 saccade as best they can to any stimulus during the
9 test. This suppression is uncomfortable to achieve
10 and also causes a subconscious distraction that
11 reduces the patient's accuracy on an already
12 difficult task. Most auto perimeters offer two basic
13 types of test. In one type the stimuli are presented
14 at levels which are just below or just above the
15 expected threshold at a given point and the test is
16 repeated for each point in a "staircase" where if
17 the previous stimulus for a given point caused a
18 patient response then the next stimulus would be
19 presented at 2 to 3 times the desired amplitude
20 resolution below the previous stimulus, and so on
21 till the stimulus fails to generate a patient
22 response. Then a further stimulus is presented
23 halfway between the brightness of the last stimulus
24 that caused a response and the stimulus that failed
25 to cause a response. The final threshold value is
26 then set depending on whether or not the patient
27 responds to this stimulus. Obviously if the patient
28 had failed to respond to the first stimulus in the
29 sequence the next stimulus would be brighter rather
30 than dimmer and the overall sequence would be the
31 reverse of the above. Clearly this method takes a
32 long time, as each point in the retina will

1 typically need five stimuli to determine the
2 threshold. Most auto-perimeters offer an alternative
3 so called "supra threshold" test where each point in
4 the retina is presented at an amplitude calculated
5 on the basis of demographic ophthalmic data to be
6 just above the expected threshold for each point
7 thus a basic plot of areas below a chosen threshold
8 can be plotted. This method is relatively crude of
9 course and does not provide any detailed contour
10 data of the threshold sensitivity.

11
12 As will be obvious from the above, the stimuli are
13 inherently presented in the above tests at or close
14 to the patient threshold. Since the total energy of
15 the stimulus is critical this means that the stimuli
16 are either very dim or of very short duration. In
17 both cases the patient is required to respond
18 consciously to stimuli that in practice are
19 extremely ambiguous. The patient will constantly be
20 marginally aware of stimuli and be consistently
21 uncertain as to whether or not they "saw" a
22 stimulus. Patients report that this is extremely
23 stressful. Practice improves the patient's
24 confidence and so the reliability of the test but
25 such practice is not practical for a routine
26 diagnostic test. The test is further compromised
27 because it is inherently difficult to fixate on a
28 single point accurately. This has two consequences.
29 Clearly if the fixation point is uncertain, then the
30 positional accuracy of any test point on the retina
31 is equally uncertain; but the problem is made worse
32 by the fact that the eye's small movements around

1 the fixation mean that the total time a given
2 stimulus illuminates a given point on the retina is
3 variable and so the total integrated energy on that
4 point varies far more than is desirable. The above
5 issues are described to clarify the nature of the
6 present invention.

7

8 In the present invention the threshold of the retina
9 is determined by the delay between the presentation
10 of a stimulus and the triggering of a reflex saccade
11 to that stimulus. If the stimuli are of low
12 brightness then this time delay will include a
13 period of integration to the point where sufficient
14 energy has been delivered to the retina to pass the
15 threshold and a further delay caused by the
16 Pullfrich effect which makes a brighter stimulus
17 travel faster through the nerve path than a dimmer
18 stimulus. If the stimuli are of higher brightness
19 then the integration time will be shorter and the
20 Pullfrich delay will also be shorter because once
21 the retinal threshold is passed the energy is still
22 integrating on the retina and so the brighter
23 stimulus will travel through the nerve path very
24 much faster. This means that varying the brightness
25 of the stimuli will vary the average time of the
26 saccade response and so the resolution of the
27 amplitude measurement is determined by the
28 resolution of the measured time increment and the
29 chosen brightness. In principle it would be assumed
30 therefore that a dimmer stimuli set would provide a
31 more accurate measure of the retinal amplitude
32 sensitivity as a function of time. While this is

1 true to an extent, the present invention aims to
2 achieve a more accurate spatial plot as well as a
3 more accurate amplitude plot. It is central to this
4 invention that the accuracy of the eye fixation is
5 superior for a few hundred milliseconds post saccade
6 to its accuracy over a longer time therefore the
7 time resolution of the measurement must be balanced
8 against the deteriorating accuracy of the fixation
9 over time. Additionally if the test is delivered
10 close to the normal visual scanning saccade
11 frequency of between 1.2 and 5 saccades per second
12 the test will feel even more comfortable and natural
13 for the patient.

14

15 Thus in simplified terms, ignoring the integration
16 loss and limit and the precise function of the
17 Pullfrich delay which will be clarified later, the
18 time T between the commencement of a stimulus point
19 and the resulting saccade of the eye to that
20 stimulus is expressed by the function

21 Eq1:

$$22 \quad T = \frac{(t^2 \cdot l + P)}{(t \cdot l)}$$

23 where t is the total time for the luminance "l" to
24 integrate to the detection threshold of the retina
25 and P is the Pullfrich delay for an arbitrarily
26 chosen luminance "h" where $h=t \cdot l$.

27

28 t can be derived from the function:

29 Eq2:

$$\left[\frac{-1}{(2 \cdot l)} \cdot \left(-T \cdot l + \sqrt{T^2 \cdot l^2 - 4 \cdot l \cdot P} \right) \right] = t$$

Naturally the greater of the two solutions is the true result since clearly the arbitrarily chosen luminance is chosen to be greater than "l". Hence for any given level of light used as a stimulus the integration time t to h can be determined from the total time T. This means that relative sensitivity of the retina from one point to another is expressed directly as a function of t and can be derived from the interval time T and the resolution of the measure can be adjusted by increasing "l". The overall speed of the test and the average time between saccades can be adjusted for maximum comfort and accuracy by adjusting l to meet the criterion of average saccade time of between 200 and 800 ms described above.

The resulting value of t can be used directly to plot a relative sensitivity map of the retina. However, often it will be required to translate these relative values to commonly used units of measure of the retinal threshold sensitivity. In that case the functions of the retinal integration and the true function of the Pullfrich delay become important. A useful optional feature of the invention is that the stimulus can be increased or decreased in brightness from its initial presentation brightness, such an increase or decrease can be used to modify the function of T to

1 t to make the resulting function either more or less
2 linear as desired. Clearly in the absence of this
3 feature the dynamic range of the test would be
4 limited if the time intervals are limited as
5 required to maintain a natural rhythm. Increasing
6 the stimulus brightness during presentation is of
7 particular use in the testing of a subject with
8 known defects since the stimuli can be rapidly
9 increased in brightness once a predetermined
10 threshold is passed, thus speeding up the test on a
11 subject who would otherwise register a large number
12 of missed stimuli or take so long for each stimulus
13 that the natural comfort rhythm is broken.

14
15 The retinal integration function is quite complex as
16 discussed by T E Cohn of Berkeley in his paper
17 "Integration by the human eye; implications for
18 warning signal design". In the typical embodiment
19 of the invention the retinal integration to
20 threshold can be taken as above which follows the
21 standard Bloch's Law which states that the product
22 of intensity of a brief flash of light times the
23 time it is on is a constant at threshold. Beyond
24 Bloch's integrating time, usually taken as 0.1sec,
25 threshold declines only modestly as duration
26 increases until, for long durations, threshold is a
27 constant. This can be enhanced by a simple two-
28 limbed approximation to this threshold function
29 which obeys Bloch's law for short durations and
30 obeys the relation that threshold is constant for
31 longer durations. This is The Blondel-Rey law. It
32 is a simple way of summarising this two-limbed

1 function. It states that the product of a flash
2 intensity times its duration is equal to the
3 asymptotic threshold value times the sum of the
4 duration plus a visual response time constant
5 described above.

6
7 In certain embodiments of the invention where longer
8 time intervals are desired it may be considered
9 worthwhile to improve the accuracy of the system by
10 utilising the more accurate Blondel-Rey law, however
11 the error induced by the use of the less accurate
12 Bloch's Law at the ideal timing intervals
13 recommended for the method are in practice less than
14 errors due to the reflex variables in the eye and
15 so, while the overall error budget can be reduced by
16 the use of the most accurate integration formula,
17 the accuracy of the Bloch Law embodiment is still
18 substantially better than that achievable by the
19 staircase method in conventional auto perimetry.

20
21 The Pullfrich function is essentially linear
22 provided the stimuli are of sufficient brightness to
23 exceed threshold in less than 400 ms, so again the
24 best performance of the system will be achieved at
25 or close to the natural saccade rhythm of the eye in
26 scanning mode. This natural rhythm has been
27 determined by the inventors in a study of over 150
28 individuals to approximate, to within 20 ms, a value
29 defined as the subject's "natural counting rhythm".
30 It is well known that people tend to count much
31 faster than once per second and so various word
32 delays are recommended to lengthen the counting

1 rhythm to approximate a second more accurately when
2 people desire to time an event without a watch. The
3 inventors speculated that the natural rhythm would
4 inherently be proportional to the subject's
5 conscious reaction time. It proved to be that a
6 person's expressed maximum comfort zone in terms of
7 saccade frequency exactly matched the subject's
8 natural counting frequency to within 20 ms. This
9 proved to be true despite a variation of well over a
10 factor of two in different individuals' natural
11 counting rhythm and also to a similar variation for
12 a given individual in different states of fatigue or
13 arousal. This fact can be used by a practitioner
14 using the invention to set the ideal brightness of
15 the basic illumination level of the stimulus by
16 asking the patient to count up to ten or count aloud
17 the number of items on a screen presentation. The
18 faster the patient counts the brighter the basic
19 stimulus should be for maximum comfort in the test.
20 Alternatively the practitioner can use the count
21 test to determine the patient's level of anxiety and
22 arousal and may take steps to calm the patient until
23 they demonstrate a slower count rhythm and so allow
24 a slower and therefore higher resolution test.

25

26 It should be clear from the above that the accuracy
27 of the test can be enhanced by repeating the test
28 with different basic illumination levels, since the
29 threshold value for a given point and the
30 integration time should correlate exactly. In
31 general, however, it would not be necessary to
32 repeat the entire test; rather the test points for

1 any anomalous areas can be tested again at a
2 different brightness and the integration time
3 measured for that brightness can be correlated with
4 the original data. If the two values agree then the
5 value is certain: if they disagree a further test at
6 either of the two previous brightness levels or
7 alternatively at a third brightness level can be
8 applied. If this third test yields anomalous results
9 then the data should be discarded for that point but
10 in practice this occurs in less than one percent of
11 the test points.

12
13 A modified sequence of test stimuli can be presented
14 to create very high spatial resolution plots of a
15 defect perimeter. This is achieved by presenting a
16 sequence of stimuli in a line crossing the perimeter
17 defect alternating with randomly placed stimuli
18 elsewhere to prevent the patient recognising the
19 pattern. In a preferred embodiment at least some of
20 the alternate stimuli are placed to plot a line to
21 cross other suspected defect perimeter zones. In
22 this latter case there should be at least four plot
23 zones randomly sequenced or, if less than three
24 suspect zones exist, then one or more random stimuli
25 should be presented. It should be noted that such a
26 line of fractional degree difference plot points
27 would be impossible with a conventional central
28 fixation perimeter since the spatial pattern of the
29 plot points would be immediately apparent to the
30 patient. Conversely in the present invention each
31 stimulus that generated a saccade becomes the new
32 fixation point. Combined with the alternating random

1 or alternate zone stimuli this makes the overall
2 spatial pattern perceived by the subject entirely
3 random and unpredictable because, although the
4 stimuli are indeed occurring repeatedly on similar
5 points on the retina, the overall spatial position
6 of the stimuli as perceived by the subject is not
7 repeating.

8
9 In recent years an alternative to basic static
10 automated perimetry has been the frequency-doubling
11 test. One example of this method uses a stimulus
12 that consists of light and dark bars of a low
13 spatial frequency (0.25 cycle/degree), flickering in
14 counter phase at a high temporal frequency (25 Hz).
15 Briefly, the flickering produces an illusion of
16 doubling the spatial frequency of the stimulus. The
17 contrast of the stimulus is gradually increased and
18 the examined subject has to indicate when a movement
19 is perceived anywhere in the visual field. The
20 method is assumed to measure the integrity of a
21 particular subgroup of retinal ganglion cell,
22 sensitive to motion. This type of stimulus can be
23 used with the disclosed saccade trigger in a
24 sequence as described for the point stimulus above
25 where the stimulus changes to the fixation point
26 with each saccade. In this case again the absolute
27 threshold function for the contrast of the bars will
28 correlate to the time T as above and hence the range
29 of contrast needed for each presentation of the
30 frequency doubling stimulus target can be reduced,
31 because the stimulus need not initially be presented
32 below the contrast threshold since the time for the

1 saccade to the stimulus will indicate the relative
2 level above threshold of the contrast.

3

4 In a further embodiment of the invention the
5 relationship between the comfort frequency of the
6 scanning saccade and the normal human visual search
7 saccade frequency can be used to determine if an
8 individual has defects in the retina by presenting
9 each eye individually with pictures based on
10 principles laid out in detail below. These pictures
11 can be natural images or computer generated images
12 with selected regions of high and low spatial
13 frequency in addition to certain visual cues that
14 the inventors have defined which allow the priority
15 of a typical initial search saccade sequence to be
16 reliably predicted. Because in these special images
17 the initial gaze direction of the eye can be
18 predicted with a high reliability, and at least the
19 first saccade from that initial gaze fixation can
20 also be predicted, it means that in viewing these
21 images the presence of a high spatial frequency
22 feature on the image will cause the eye to be
23 attracted to it after the initial high priority cue
24 subsequent to the primary gaze fixation. In the
25 normal eye only the blind spot exists as an area
26 that obscures a feature that is revealed to the eye
27 when this initial saccade occurs. If an area of high
28 spatial frequency is revealed as the blind spot
29 moves this causes a change in both the saccade
30 priority AND causes the natural scanning rhythm to
31 "reset" to initial search mode. Since the initial
32 search saccade frequency is much more rapid than the

1 natural scanning frequency, any region of high
2 spatial frequency or other high priority cue
3 revealed as the eye initially saccades causing a
4 defect to cease to obscure the said cue will cause a
5 second burst of high frequency saccades as the eye
6 attempts to accommodate for its lack of expected
7 peripheral vision definition by scanning the
8 revealed cues with the fovea. This is an especially
9 useful test since it detects even quite shallow
10 anomalies in the eye even if the contrast
11 differential of the image is much higher than the
12 anomaly depth. The images are designed to cause
13 scanning saccades of relatively small amplitude but
14 the presence of an anomaly will cause a large
15 amplitude saccade as the fovea moves to accommodate
16 as described above, and hence both the frequency of
17 the saccades and the amplitude can be used to signal
18 the presence of an anomaly. In this case time from
19 the initial saccade to the triggered saccade is
20 inversely proportional to the depth of the saccade
21 because the differential between the anomaly and the
22 normal portion of the retina is equivalent in
23 practice to the contrast or differential above
24 threshold described for the previous tests in terms
25 of the relationship between stimulus and the speed
26 of the saccade reflex. The location of the saccade
27 spatial frequency cues can be set in a sequence of
28 images to digitally sequence the areas of interest
29 on the retina. For example eight images presented in
30 sequence can detect the presence of an anomaly one
31 64th of the visual field for each eighth of the
32 visual field tested in each image. Theoretically

1 this could be further refined by further subdivision
2 but in practice it is probably better to revert to
3 either frequency doubling or constant stimulus
4 plotting if detailed plotting is desired. This image
5 test is best used as an "instant" detector of the
6 presence or absence of anomalies worthy of more
7 detailed diagnosis.

8

9 Depending on the desire of the practitioner the
10 image colours can be chosen to cover either the full
11 spectrum or selected colours such as blue and yellow
12 that preferentially shows cone anomalies and is
13 therefore more sensitive to relatively small
14 pathologies of the eye.

15 The basic rules of the image design for predicted
16 priority sequence are as follows:

17 A solid perspective cue such as road, path or river
18 with a dark end point will draw the first gaze
19 fixation. This will be followed immediately by a
20 saccade to the darkest area of the image coupled
21 with any high spatial frequency data followed by a
22 saccade to the next highest spatial frequency region
23 that is also dark or to the highest spatial
24 frequency area of any brightness if there are no
25 more apparently dark areas of the image. These cues
26 should be set at least ten degrees apart. In a
27 normal vision subject these initial three saccades
28 will occur in less than 400 ms followed by much
29 slower "count" frequency saccades of less than 10
30 degrees amplitude as the eye assumes normal scanning

1 mode. If however any area of the eye has a defect
2 that uncovers an area of high spatial frequency then
3 the image effectively re-triggers the eye/brain
4 system to repeat the initial search sequence and so
5 the high frequency high amplitude saccades will
6 continue for at least twice the duration of a normal
7 vision subject.

8
9 Figs. 2 and 3 show representative figures as an
10 example to clarify the principles of the images.
11 Note that the real images may be computer generated
12 photo realistic images or abstract images. The
13 critical aspect is that they follow the principles
14 laid out here.

15
16 In Fig. 2, the first fixation is marked as 1 the
17 dark area at the end of the "perspective suggesting"
18 path. The area of the retina effectively under test
19 is 3 and the second fixation attractor is 2. In a
20 normal vision subject the spatial frequency
21 attractor at 3 does not change during the saccade
22 from 1 to 2 and so does not cause an immediate
23 saccade whereas if a defective area of the retina
24 obscured the high spatial frequency attractor at 3
25 when fixating on 1 then it would "appear" to the eye
26 immediately after the saccade to 2 and so trigger a
27 reflex saccade. It should be noted that should the
28 subject in fact saccade instead to 3 instead of 2
29 after 1, this obviously by definition demonstrates
30 that 3 was not under a region of low sensitivity or
31 resolution. This means that this type of test is

1 uniquely free from false positive results which is a
2 great advantage in any screening diagnostic test.

3 Fig. 3 illustrates the test being repeated for a
4 subsequent field.

5 A sequence of images covering the entire field
6 sector by sector can be presented to the patient.
7 The high spatial frequency sector should be no
8 greater than 0.25 degrees per cycle for the areas
9 outside the central ten degrees from the fovea.
10 Ideally the high spatial frequency sector should be
11 more than twice the average spatial frequency of the
12 rest of the image and regions less than half the
13 average spatial frequency should be avoided, as this
14 can tend to alter the saccade priority from the
15 ideal.

16 It should be noted that although the term
17 "perspective" is used this is not intended to mean
18 necessarily true perspective image. The human vision
19 system is so tuned to seek perspective cues that any
20 apparent taper however distorted will tend to be
21 read as a perspective cue. This has been shown in
22 our research to be almost always the primary cue in
23 an image since the brain seeks a sense of scale in
24 any image with an extremely high priority. However
25 areas that suggest shadows or doorways that may
26 obscure potential threats are very high priority
27 too. This proved to be so even with very young
28 subjects; the inventors suspect this is a
29 fundamental survival trait that is as genetically
30 programmed as the blink reflex is to an apparent
31 direct threat to the eye. The combination of a

1 "suggested perspective" cue and a dark "doorway" cue
2 is virtually 100 percent reliable as a trigger of
3 the first gaze fixation. In fact no subject in the
4 test trials ever failed to fixate first on such a
5 cue. Note that since the eye saccades to that first
6 cue from its previous rest position no feature of
7 the image is processed by the brain until after the
8 primary gaze fixation.

9 There are many other cues that the inventors have
10 researched that can be arranged in suitable priority
11 sequences to lend further variety to the test but
12 the above listed are adequate to create a successful
13 visual field defect diagnostic tool as disclosed
14 herein.

15 It should be obvious that instead of a sequence of
16 still images a moving image of many frames per
17 second could be used provided the said moving image
18 could be divided into two or three second sequences
19 where the saccade priorities of each such sequence
20 were known as above. In such a moving image method
21 stimuli that may cause the eye to enter pursuit mode
22 should be avoided.

23 In an alternative method a moving image sequence can
24 be used which is designed to exploit the pursuit
25 mode. In that case the pursuit stimulus should be
26 considered the primary fixation. Wherever the
27 pursuit stimulus comes to rest on the screen can be
28 defined for the still images above. In this case the
29 timing period used to discriminate considered as the
30 primary gaze fixation with the second and third
31 priority cues as normal from abnormal eye behavior

1 should be 2 to 3 second sequences free of the said
2 pursuit stimuli.

3 The apparatus may also be used to test for dyslexia
4 using the Fischer method of determining whether and
5 how well the patient is capable of reverse saccades
6 where the patient is instructed to saccade in a
7 direction OPPOSITE to the stimulus. In this
8 invention the method of the test is a presentation
9 of an image of for example the surface of a rabbit
10 warren. The patient is told that a dot will appear
11 just before a rabbit appears exactly opposite from a
12 moving fixation point and they must identify the
13 rabbit from a group of three recognisable "bunnies".
14 The fixation point is for example a bird or fox
15 image moving across the screen at any angle. A red
16 or other colour bright dot appears at some point and
17 within 50ms a rabbit appears for 100 to 150 ms
18 exactly opposite to the dot as measured through the
19 fixation stimulus. Normal subjects will in the
20 majority of cases register one saccade whereas
21 dyslexics will in general register two, one for an
22 aborted saccade to the initial stimulus they are
23 told NOT to look at and one for the correction to
24 the rabbit. This is because the ability of the
25 cognitive system to override the reflex to saccade
26 to any stimulus has proven to be consistent with the
27 absence of dyslexia whereas the inability to
28 override has proved to be an indication of the
29 opposite. In this invention the proposed
30 "recognition of the rabbit task" or similar
31 recognition task is a strong incentive to saccade as
32 early as possible to see the "rabbit" long enough to

1 recognise it. It is critical to the invention that
2 the features of the rabbit or other recognition task
3 that differentiate it from the other samples
4 previously shown with it to the subject must be of
5 such fine detail as to only be visible to the fovea.
6 If the person waits till the "rabbit" appears before
7 saccading then the saccade will arrive too late for
8 the brain to have time to image the rabbit
9 adequately for recognition. Hence simply suppressing
10 the reflex response to the red dot stimulus is not a
11 solution to the task. Only if the subject saccades
12 opposite to the stimulus will the subject be looking
13 at the point where the rabbit appears and so get
14 enough time with the rabbit imaging on the fovea to
15 allow recognition. This requires that the eye is
16 capable of saccading at near reflex speed in the
17 opposite direction to the stimulus. This task is
18 possible at about 75 to 90 percent of the time for a
19 normal individual above the age of five. It is
20 impossible for children aged three or less and it is
21 virtually impossible for even mild dyslexics. For
22 example the set of rabbits in the test might be
23 drawn with one two or three sets of whiskers with an
24 apparent diameter of 0.1 to 0.3 degrees. In such a
25 case only the fovea would have sufficient resolution
26 to perceive the whiskers well enough to count them.

27

28 In a further embodiment of the invention, means are
29 provided to illuminate the eye preferably in the
30 infra red region capable of creating a clear
31 highlight on the cornea as viewed by a camera and
32 means whereby the camera delivers images in an

1 electronically interpretable way to a calculating
2 device such that the highlight reflections of the
3 cornea of both motion blurred and non blurred images
4 may be analyzed by commercially available software
5 algorithms to determine the angular moment of the
6 blur which in turn defines the direction of the
7 eye's movement causing the motion blur. Such means
8 are used to interpret the saccade results to confirm
9 that the saccades were induced by the stimulus and
10 not other distraction.

11
12 The test data can also be compared with a library of
13 data categorised for factors including age that
14 affect the normal sensitivity of the retina and a
15 second database of diseased and other abnormal
16 retinal data that may be compared to the measured
17 retinal data with a view to allowing a software
18 algorithm to suggest a possible diagnosis based on
19 said similarity by means of superposition of
20 perimeter and sensitivity data for each defect on
21 images of perimeters stored in the database of
22 diseased and other abnormal retinal data.

23
24 This can be done by assessing geometric
25 similarity to a set of images where the set
26 contains a majority of data from a given
27 disease or other abnormal category would
28 trigger the algorithm to suggest the majority
29 disease as the probable diagnosis, such
30 majorities being passed to a second database on
31 confirmation of the said diagnosis over time.
32 This second database is a refined rapid search

1 evolved version of the first database that may
2 be used preferably to the first when it exceeds
3 a sample size of at least 4 times the average
4 majority sample size.

5 Improvements and modifications may be incorporated
6 without departing from the scope of the invention as
7 defined in the claims appended hereto.